Application of Evidence Theory in Radiation Oncology Outcome Analysis

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***Abstract*— In this paper, we apply the Dempster-Shafer theory to outcome analysis in radiation oncology. Evidence from different sources, some of them inconsistent, is combined by Dempster's rule to provide an innovative method for radiotherapy outcome analysis.**

Keywords-evidence; Dempster-Shafer theory; radiation oncology; pneumonitis

I. INTRODUCTION

Evidence-based medicine has become the foundation of radiation oncology development. There are different levels of evidence upon which radiation therapy practice is based. These include level I evidence, which is from adequately powered, high quality randomized trials with meta-analysis of randomized trials showing statistically consistent results; level II, from randomized trials that are non-adequately powered, possibly biased, or showing statistically inconsistent results; level III, non-randomized studies with concurrent controls; level IV, which include non-randomized studies with historical controls (i.e., typical single arm phase II studies); and level V, which includes expert committee reviews, case reports, and retrospective studies. With all of this sometimes consistent, sometimes inconsistent, even conflicting, evidence, it is essential to apply appropriate methods for combining the evidence for clinical guidance. In this study, we apply evidence theory to combine evidence from different sources for better prediction of the outcome. This application of evidence theory has the potential to change the way outcome analysis is performed. A case study of the "degree of belief" and "plausibility" in regard to the occurrence of pneumonitis in radiation therapy is implemented as an example to demonstrate our application of evidence theory.

II. FUNDAMENTALS OF DEMPSTER-SHAFER THEORY

Dempster-Shafer theory, also known as evidence theory, is a mathematical theory of evidence and plausible reasoning. The theory was developed by Glenn Shafer in 1976 [1] based on earlier work of Arthur Dempster [2]. In a finite discrete space, Dempster-Shafer theory can be interpreted as a generalization of probability theory. In probability theory, evidence is associated with only one possible event, whereas in Dempster-Shafer theory, evidence can be associated with multiple possible events, i.e., set of events. The main advantages of Dempster-Shafer theory include the ease of representing evidence of different levels of abstraction and combining the effects of different bodies of evidence.

There are three important functions (or measures) in Dempster-Shafer theory: the basic belief assignment function (bba or m), the belief function (Bel), and the plausibility function (Pl). In the context of Dempster-Shafer theory, a sample space is called a universal set or frame of discernment, and its power set is denoted by 2^θ. A basic belief assignment over a frame θ is a function $m: 2^\theta \to [0,1]$, satisfying the following two conditions:

$$\begin{aligned} m(\phi) &= 0 \\ \sum_{A\subseteq\theta} m(A) &= 1. \end{aligned} \tag{1}$$

The belief function is defined in terms of the bba's as follows:

$$Bel(A) = \sum_{B\subseteq A} m(B), \tag{2}$$

where the sum is over all subsets of A. The plausibility function is defined as

$$Pl(A) = \sum_{B\cap A\neq\varnothing} m(B). \tag{3}$$

In order to combine evidence from different sources we apply Dempster's rule of combination. Dempster's rule combines multiple belief functions through their basic belief assignments. These belief functions are defined on the same frame of discernment, but are based on independent sources. Specifically, the combination is calculated from the two sets of bba's, m_1 and m_2, in the following manner:

$$m_{1,2}(A) = \frac{\sum_{B\cap C=A} m_1(B)m_2(C)}{1-\sum_{B\cap C=\varnothing} m_1(B)m_2(C)}. \tag{4}$$

In general, for multiple sources the combination rule reads,

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$$m(A) = \frac{\sum_{\bigcap A_i = A} \prod_i m_i(A_i)}{1 - \sum_{\bigcap A_i = \varnothing} \prod_i m_i(A_i)}. \quad (5)$$

The construction of a universal set, its power set and m-functions, and quantifying uncertainty of model prediction and fusing multiple models for improved prediction in the context of applications are discussed in [3] and [4].

III. Plausibility of Pneumonitis in Radiation Therapy

Radiation pneumonitis is a lung inflammatory process that follows radiation therapy of tumors in and around the thorax. This condition develops in approximately 5-50%, 5-10%, and 1-5% of patients irradiated for cancers of the lung, mediastinal lymphatics, and breast, respectively [5, 6]. Reference [7] reviews the probability of radiation pneumonitis as a function of mean dose to the lung. This reference included the results from ten different institutions. Large variations are observed in the results from different institutions. For instance, probabilities of pneumonitis range from 12% to 30% for the mean lung dose of 20Gy. This evidence from multiple institutions may be combined by Dempster-Shafer theory to estimate the lower and upper probabilities of pneumonitis at a certain dose. This case is used as an example to describe how the Dempster-Shafer theory is applied to radiation therapy outcome analysis.

IV. Simulation Data

For the purpose of demonstration, we pose the rather simple problem of determining the lower and upper probabilities of the occurrence and non-occurrence of pneumonitis due to radiotherapy of 20 Gy mean lung dose level. We use the data from the three institutions of the ten mentioned in Reference [7]. To apply the tools of evidence theory, a universal set (frame of discernment) is constructed with two elements, A and B, representing respectively the cases of pneumonitis complication and non-complication following radiotherapy. The judgment based on the three institutions data (in terms of probability) supporting A and B is given in Table 1. This judgment is subjective in that it takes into account in a sense the confidence interval associated with the probability distribution versus mean lung dose (obtained through processing of data with traditional statistical approach).

TABLE I. THE SIMULATION DATA USED IN THIS STUDY

Evidence Sources	Probability[a] of complication	Probability of non-complication
Institution-1	0.12	0.6
Institution-2	0.18	0.65
Institution-3	0.3	0.5

a. Probability of pneumonitis is evaluated at the mean lung dose of 20Gy

It may also draw upon decision-maker's domain knowledge and trained intuition. It explains why the sum of the probability of complication and the probability of non-complication is not unity.

V. Combination of Evidence

In this section, using Dempster's rule of combination, we rationally combine the evidence from the three independent institutions in Table I.

In the present instance, the universal set is $\theta = \{A, B\}$, where A represents the subjective probability of radiation pneumonitis and B is the subjective probability of the absence of pneumonitis. The associated power set is $2^\theta = \{A, B, \theta, \phi\}$ where ϕ is the null set. Using the data of Table I and the definition of basic belief assignment function, the *m*-functions corresponding to the three institutions are

$$m_1(\{A\}) = 0.12,\ m_1(\{B\}) = 0.60,\ m_1(\theta) = 0.28;$$
$$m_2(\{A\}) = 0.18,\ m_2(\{B\}) = 0.65,\ m_2(\theta) = 0.17;$$
$$m_3(\{A\}) = 0.30,\ m_3(\{B\}) = 0.50,\ m_3(\theta) = 0.20.$$

Using Eqs. (2), (3) and (5), it is straightforward to obtain the combined belief and plausibility functions for A and B (reported in Table II) which provide the probability range $Bel(A) < P(A) < Pl(A)$. The probability ranges for complication and non-complication are [0.106, 0.123] and [0.876, 0.893], respectively. It is to be noted that Dempster's rule of data fusion (which may be considered as a generalization of the classical Bayesian inference) has narrowed down the probability range by strengthening agreements and weakening conflicts.

TABLE II. BELIEF AND PLAUSIBILITY FUNCTIONS

	Bel	***Pl***
A	0.106	0.123
B	0.876	0.893

VI. Conclusion

In this paper, we have studied a simple example to demonstrate how the evidence theory tools can be used to aid an oncologist in his decision process. It will really be of value in aiding the decision process in complex situations, such as radiotherapy dose determination maximizing cancer control while minimizing harmful side effects. This is the subject of our continuing studies.

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